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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TURNER, SHARON L	
ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/723,713	SCHENK, DALE B.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication app ars on th cover sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 November 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. The amendment filed 9-26-02 has been entered into the record and has been fully considered.

2. Claim 33 is amended. Claims 33-34 are pending.

Priority

3. As set forth in the Action of 3-26-02, Applicant's claims for domestic priority under 35 U.S.C. 119(e) are acknowledged. However, the provisional applications (60/067,740 filed 12-2-1997 and 60/080,970 filed 4-7, 1998) upon which priority is claimed were filed more than 12 months prior to the filing date of the parent application (09/322,289 filed 5-28-1999) and thus fail to comply with the requirements for priority under 35 U.S.C. 119(e). Thus, the effective filing date is that of 09/322,289, filed 5-28-1999. If there is an intervening priority application to which applicant's are entitled benefit, it should be claimed in order to provide continuity with the provisionals.

Applicant's argue in the response of 9-26-02 that a new application data sheet has been submitted entitling applicants to the December 2, 1997 priority application through application 09/201,430.

However, if applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No.

_____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. In instant case, there is no reference to the '430 application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c).A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions,Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Drawings

4. The drawing of Figure 11 is objected to because the figure lacks an appropriate legend which indicates the peptide treatment groups as indicated and described in the

figure and specification, see in particular pp. 62-63 and brief description of the drawings, p. 7. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Applicants may alternatively choose to amend the brief description of the drawings so that it clearly reflects the groups represented in the Figure. Such amendment would be considered an appropriate correction so as to obviate abandonment of the application.

Information Disclosure Statement

5. The information disclosure statement filed 10-9-01 and 8-21-02 contains particular references which fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because they lack a relevant public availability date. Those references have been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 33-34 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the decision of The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398 (CAFC 1997), the court held that:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

The specification fails to disclose any nucleic or amino acid sequences. In particular, no sequences which specifically encode either the heavy or light chains of an antibody which would specifically bind to an amyloid deposit.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

Thus, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic and amino acid sequences and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or

simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific nucleic and amino acids are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Applicants argue that the PTO's written description guidelines with respect to antibodies (Example 16) allows for functional terms without sequence information because of the routine art-recognized method of making antibodies to characterized antigens, the well defined structural characteristics for the five classes of antibodies, the functional characteristics of antibody binding and the fact that antibody technology is well developed and mature. Applicants further argue that the cases cited are distinguished from the instant facts in that no issue of new matter is raised and that the issue is not one of cloning a new gene but for use of nucleic acids encoding a class of antibodies to a well characterized antigen. Applicants assert that adequate written description is provided by the recitation of a well characterized antigen, conserved features of antibodies and the mature state of the art as provided by the written description guidelines.

Applicant's arguments filed 9-26-02 have been fully considered but are not persuasive. Applicants claims are directed to administration of a polynucleotides encoding at least one antibody chain, whereby the polynucleotide is expressed to produce the antibody chain and the antibody chain is effective to reduce levels of Aβ in

the brain of the patient. Thus, the claims differ from the written description guidelines which are directed to the written description of an antibody molecule and not to the nucleic acids encoding them. The artisan is not well versed in predicting those nucleic acid sequences which encode variable regions capable of binding any particular epitope, even for a defined epitope as the variable region of the antibody which binds it is unrelated to the sequence to which it binds. Moreover, the nucleic acids encoding such antigen recognition sites vary amongst different antibodies and the antigens they are reactive to, see for example Castellani et al., Am. J. of Pathol., Nov. 2002, 161(5):1695-700 and Taki et al, Biosci. Biotech. & Biochem., May 2001, 65(5):1082-89. Thus, none of the characteristics which applicants refer to as being well developed or established in the antibody art are shared for the description of nucleic acids that encode them. While the artisan may experimentally determine the variable region sequence for any particular antibody using recombinant DNA techniques, what is required of the claim is a description of those nucleic acids which when suitably expressed in the patient produce an antibody capable of effective treatment or prevention of disease characterized by amyloid deposits via reducing Aβ levels in the brain. However, no such nucleic acids are provided by the specification. Moreover, only particular antibodies have been shown as being capable of exhibiting such plaque removal. Applicants argue that description of the antigen is sufficient. However, description of the antigen fails to delineate the nucleic acid structure capable of producing an antibody that recognizes it or the particular antibodies which are capable of removing amyloid plaques within the brain. Thus, there are no disclosed structures capable of providing the recited function. Thus the lack of description of means (nucleic acids) for achieving the desired effects (treatment and prevention of amyloid

deposit diseases) lacks sufficient written description to evidence that applicant's were in fact in possession of the claimed subject matter drawn to a genus of polynucleotides.

8. Claims 33-34 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears (as drawn to canceled claim 1) to be drawn to a method of preventing or treating disease via in vivo nucleic acid expression of recombinant antibody molecules. However, as noted by Peterson et al., 1996 Feb., Lab. Animal Sci., 46(1):8-14, p. 9, column 1, last paragraph, lines 4-6, "because of their (antibodies) large size and difficulty in proper protein folding, functional complete immunoglobulin molecules could not be produced in bacteria." The specification fails to exemplify the particular nucleic acids essential to encode the relevant antibody molecule and fails to teach the essential methods of expression in a host cell, particularly in a patient as the claim is drawn. Further, the claim encompasses the prevention or treatment of any disease associated with amyloid deposition. However, the specification only discloses antibody capable of binding beta-amyloid and which may be useful in decreasing amyloid burden in brain. Yet the output measurement fails to correspond to the activities noted in the claim 1, i.e., an antibody capable of preventing or treating a disease characterized by amyloid deposit in a patient. The clinical and neuropsychological manifestations of Alzheimer's are reflected in Morris et al., Neurology, September 1989, 39:1159-65. Yet the specification fails to show the amelioration, treatment or prevention of any clinically symptomatic measurement of Alzheimer's as disclosed. Thus, the skilled artisan would be forced into further undue experimentation not only to determine a method of antibody delivery via nucleic acid but

to verify and determine the relevant antibodies and any clinically relevant effects which are either treated or prevented via such treatment for any particular amyloid deposition disease, inclusive not only of beta-amyloid deposition in Alzheimers, but of amyloid deposition for example in amyloid angiopathy of the vascular or immune systems.

Thus, in view of the lack of guidance in the prior art, lack of examples, and lack of predictability in treatment of diseases, one skilled in the art would be forced into further undue experimentation to determine those antibodies relevant to the particular method, i.e., which are capable of preventing or treating a disease characterized by an amyloid deposit in a patient, to determine the relevant antibodies' amino and nucleic acid sequences, and further determine a means of expression in a patient such that the nucleic acid administered to the patient actually produces and "administers" the antibody as claimed.

Applicants argue that Peterson is directed to expression of anibodies in bacteria and not in patients and that because patients naturally express immunoglobulins that such difficulties would not be expected. Applicants further argue that the specification exemplifies several antibodies which bind Aβ, that it would be routine to produce other antibodies and that the artisan would be able to sequence and/or amplify the variable regions from these antibodies. Applicants further argue that the specification at pp. 25-26 teaches a number of well known regulatory elements and delivery vectors that can be used. Applicants have amended the claims to be directed to treating a disease characterized by amyloid deposit comprising Aβ peptide. Applicants further argue that the specification shows reduction of Aβ depositions in the brains of transgenic animals treated with anti-Aβ antibodies and that Morgan and Janus teach the correlation of improved cognitive effects with such reductions and that Morris supports diagnosis by histopathological examination.

Applicant's arguments filed 9-26-02 have been fully considered but are not persuasive. While Peterson is directed to expression in bacteria, Peterson exemplifies the difficulties encountered in expression of antibody molecules via nucleic acids. However, even in patients, the nucleic acid molecule must be appropriately targeted as not all human cells naturally express immunoglobulin molecules. In human patients only B-cells are noted to express immunoglobulins. However, the expression systems to which applicants refer at pp. 25-26 do not appear to directly target expression of antibodies via nucleic acid expression in B-cells. Moreover, the specification faills to exemplify a single example of such antibody expression within a human patient. While the specification exemplifies particular antibodies which are capable of reducing Aβ plaque deposits within brain (Aβ1-42, Aβ1-40, conjugated Aβ1-5), it is noted that not all antibodies reactive with Aβ were capable of such. Thus, the results exemplify the fact that not all variable regions capable of binding antigen are capable of effecting plaque removal. Moreover, it is the administration of antibodies which is shown by the specification and not the administration of nucleic acids capable of expressing such antibodies within the host. The specification provides no exemplification of nucleic acid expression within the human patient which produces antibodies capable of removing beta amyloid plaques within the host . Moreover, there is no basis found within the literature indicating that such expression is routine, predictive or enabled. A search of the prior art as to in vivo expression of antibody molecules via nucleic acid expression for mediating plaque removal has not revealed references which evidence enablement for the instantly claimed invention. Thus, the claims remain drawn to an invention which is not commensurate in scope with the teachings of the specification and would require further undue experimentation to define the pertinent variable region sequences, as well as to enable their effective expression within the host.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 33 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 33 remains drawn to "the patient" where no antecedent basis for any patient exists. The article "a" patient would be appropriate.

Status of Claims

11. No claims are allowed.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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Sharon L. Turner, Ph.D.

December 1, 2002